NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

DIAGNOSIS AND MANAGEMENT OF CELIAC DISEASE

GUIDELINES BEING COMPARED

1. **American Dietetic Association (ADA)**. Celiac disease (CD). Evidence-based nutrition practice guideline. Evidence based nutrition practice guideline. Chicago (IL): American Dietetic Association (ADA); 2009. Various p.
2. **American Gastroenterological Association Institute (AGA)**. AGA Institute medical position statement on the diagnosis and management of celiac disease. Gastroenterology 2006 Dec;131(6):1977-80.
3. **National Institute for Health and Clinical Excellence (NICE)**. Coeliac disease. Recognition and assessment of coeliac disease. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 May. 86 p. (Clinical guideline; no. 86). [87 references]
4. **World Gastroenterology Organisation (WGO-OMGE)**. WGO-OMGE practice guideline: celiac disease. Paris (France): World Gastroenterology Organisation (WGO-OMGE); 2007 Feb. 18 p.

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AREAS OF AGREEMENT AND DIFFERENCE

A direct comparison of the recommendations presented in the above guidelines for the diagnosis and management of celiac disease is provided in the tables below.

Areas of Agreement

NICE and WGO-OMGE agree that common symptoms of CD include: diarrhea; failure to thrive (in children); weight loss; abdominal pain, cramping, bloating or distension; persistent or unexplained gastrointestinal symptoms including nausea and vomiting; and prolonged fatigue. AGA, NICE and WGO-OMGE agree that, among others, reduced bone density, unexplained infertility, unexplained recurrent miscarriage, peripheral neuropathy, unexplained elevations in liver transaminase levels, short stature (in children), irritable bowel syndrome and microscopic colitis may also be indicative of CD. There is also agreement that there may be an elevated risk of CD in individuals with Down's syndrome, iron deficiency anemia, autoimmune thyroid disease, type 1 diabetes mellitus, Sjögren's syndrome, Turner's syndrome, and autoimmune liver conditions. None of the groups recommend population-based screening for CD, but rather recommend screening among symptomatic and/or high-risk individuals. All three groups agree that testing of first-degree relatives of individuals with CD is advisable, as there an increased risk in this population; AGA and WGO-OMGE also recommend testing of second-degree relatives.

Diagnostic Testing

The three groups to address diagnosis, AGA, NICE and WGO-OMGE, agree that positive serologic test results combined with intestinal biopsy are the gold standard for establishing a diagnosis of CD, and that a gluten-containing diet should be maintained throughout the diagnostic process (serological tests and biopsy if required). NICE specifies gluten should be eaten in more than one meal every day for a minimum of 6 weeks before serological testing.

With regard to serologic testing, there is overall agreement that routine use of antigliadin antibody tests (IgG AGA and IgA AGA) for diagnostic purposes has been supplanted by use of the anti-tTG antibody tests, specifically the IgA EMA and IgA tTG. In individuals with confirmed IgA deficiency AGA and NICE agree that the IgG tTGA and/or IgG EMA tests should be used. For all other individuals, however, AGA and NICE agree that IgA tTGA should be the first-line serologic test performed, with NICE recommending IgA EMA testing be used if the tTGA result is equivocal. If serology results are negative and CD is still suspected, AGA and NICE agree that IgA deficiency should be investigated by measurement of the serum IgA level. See Areas of Difference for WGO-OMGE recommendations.

All three groups address the disease-associated HLA alleles DQ2 and DQ8, with AGA and WGO-OMGE stating that they are a necessary but not a sufficient condition for the development of CD. There is overall agreement that while not routinely recommended, the high negative predictive value of the absence of these alleles can be helpful in excluding CD when the diagnosis based on other tests is unclear.

Management

The guidelines that address management of CD (ADA, AGA, WGO-OMGE) agree that a strict, lifelong GFD is the most effective treatment and all recommend consultation with a registered dietitian knowledgeable in GFDs. With regard to oats, ADA and WGO-OMGE agree that gluten-free oats uncontaminated with wheat, barley or rye are generally safe. All three groups recommend BMD screening in patients with CD, which ADA specifies should be done within the first

year. The groups agree that any nutritional deficiencies, most notably iron, folate, calcium, vitamin D, and vitamin B12 deficiency, should be screened for and treated using supplementation and/or dietary modification.

ADA recommends the RD assess the following factors in individuals with CD: food and nutrition related history; factors affecting quality of life; biochemical data and results of medical procedures, specifically the following profiles: gastrointestinal, nutritional anemia, vitamin, mineral, lipid, electrolyte and renal; gastrointestinal symptoms; and the presence of other disease states (e.g., thyroid conditions, other autoimmune and endocrinologic disorders and diabetes).

There is overall agreement that patient education is a key element in promoting adherence to the GFD and should include information on the nature of CD and on the GFD. ADA also recommends educating individuals with CD on reviewing ingredients on food and supplement labels, avoiding sources of gluten, and cross-contamination in gluten-free food preparation within manufacturing plants, restaurants and home kitchens. AGA and WGO-OMGE also recommend patients be referred to CD support groups both to improve knowledge of CD and the GFD, but also for emotional and social support.

Follow-Up/Persistence of Symptoms

ADA and AGA agree that continued monitoring and evaluation of dietary compliance to the GFD is essential. ADA recommends evaluation of the gluten-free dietary pattern, hidden sources of gluten, potential exposure to cross-contamination, and antibody levels. According to AGA, there are no clear guidelines as to the optimal means to monitor adherence to a GFD. They note that monitoring adherence by clinic visits and serologic testing appears to be a reasonable approach in children and adults, with the understanding that in adults a negative serologic test result does not necessarily mean improvement beyond severe subtotal or total villous atrophy.

The three groups to address follow-up, ADA, AGA and WGO-OMGE agree that the persistence of symptoms is usually caused by continued ingestion of gluten. If gluten exposure has been ruled out, the groups agree that patients should be evaluated for other potential causes, such as lactose, fructose or carbohydrate intolerance; bacterial overgrowth; microscopic colitis; pancreatic insufficiency; refractory sprue; related cancers; or other gastrointestinal diseases.

Areas of Difference

Diagnostic Testing

While AGA and NICE recommend that IgA tTGA be the first-line serologic test performed, WGO-OMGE, in contrast, recommends either IgA EMA or IgA tTG be performed first. Moreover, while AGA and NICE agree that IgA deficiency should be investigated only if initial serology is negative and CD is still suspected (in individuals without known IgA deficiency), WGO-OMGE recommends that total serum IgA level be measured at the same time that initial serologic testing be performed.

COMPARISON OF RECOMMENDATIONS	
DIAGNOSIS **Abbreviations** **Back to TOC**	
Clinical Presentation/Whom to Test	
ADA (2009)	No recommendations offered.
AGA (2006)	It is the position of the AGA Institute that testing for CD should be considered in symptomatic individuals who are at particularly high risk. These include those with unexplained iron deficiency anemia (IDA), a premature onset of osteoporosis, Down syndrome, unexplained elevations in liver transaminase levels, primary biliary cirrhosis, and autoimmune hepatitis. Situations in which testing for CD should be selectively considered during the medical evaluation, especially if symptoms that could be the result of CD are present, include type 1 diabetes mellitus, autoimmune thyroid disease, Sjögren's syndrome, unexplained recurrent fetal loss, unexplained delayed puberty, selective IgA deficiency, irritable bowel syndrome, Turner's syndrome, peripheral neuropathy, cerebellar ataxia, and recurrent migraine, as well as children with short stature and first- and second-degree relatives of patients with CD (see the original guideline document for a more detailed description of each of the high risk populations).

NICE (2009)	**When to Offer Testing**
	
	Offer serological testing for CD to children and adults with any of the following signs and symptoms:
	
	• Chronic or intermittent diarrhoea
	• Failure to thrive or faltering growth (in children)
	• Persistent or unexplained gastrointestinal symptoms including nausea and vomiting
	• Prolonged fatigue ('tired all the time')
	• Recurrent abdominal pain, cramping or distension
	• Sudden or unexpected weight loss
	• Unexplained iron-deficiency anaemia, or other unspecified anaemia
	
	Offer serological testing for CD to children and adults with:
	
	• Any of the following conditions:
	  • Autoimmune thyroid disease
	  • Dermatitis herpetiformis
	  • Irritable bowel syndrome

	• Type 1 diabetes **or** • First-degree relatives (parents, siblings or children) with CD Consider offering serological testing for CD to children and adults with any of the following: • Addison's disease • Amenorrhoea • Aphthous stomatitis (mouth ulcers) • Autoimmune liver conditions • Autoimmune myocarditis • Chronic thrombocytopenia purpura • Dental enamel defects • Depression or bipolar disorder • Down's syndrome • Epilepsy • Low-trauma fracture • Lymphoma • Metabolic bone disease (such as rickets or osteomalacia) • Microscopic colitis • Persistent or unexplained constipation • Persistently raised liver enzymes with unknown cause • Polyneuropathy • Recurrent miscarriage • Reduced BMD • Sarcoidosis • Sjögren's syndrome • Turner syndrome • Unexplained alopecia • Unexplained subfertility
WGO-OMGE (2007)	**<u>Diagnosis of CD</u>** **Key Symptoms** *Adults: Gastrointestinal Symptoms* • Chronic diarrhea (most common symptom) • Weight loss • Anemia • Abdominal distension • Lassitude and malaise *Children: Gastrointestinal Symptoms* • Failure to thrive, weight loss, down-shift of weight or height

	centile, short stature • Vomiting • Diarrhea • Recurrent abdominal pain • Muscle wasting • Irritable bowel • Hypoproteinemia • Irritability and unhappiness *Adults and Children: Nongastrointestinal Symptoms* • Iron deficiency/anemia • Dermatitis herpetiformis • Peripheral neuropathy • Folic acid deficiency • Reduced bone density • Unexplained infertility *Consider CD in Cases of*: • Unexplained folic acid, iron, or B12 deficiency • Reduced serum albumin • Unexplained hypertransaminasemia • Osteoporosis and osteomalacia • Recurrent abdominal pain or bloating • Skin rashes **Management of CD** Initial approach: • Advise serological screening for first-degree and second-degree relatives **Screening for CD** The current view is that there is not enough evidence to support a decision to carry out mass screening of the general population, nor is there enough evidence to assess the risks of undetected CD. **NGC Note**: Refer to the original guideline document for a discussion of possible differential diagnoses and populations at high-risk of celiac disease.
Diagnostic Testing	
ADA (2009)	No recommendations offered.
AGA (2006)	Diagnostic tests should be performed before the initiation of gluten restriction begins. Positive serologic test results may resolve and

histologic findings may improve with the removal of gluten from the diet. The initial detection of possible CD is probably best obtained by the use of a simple and accurate serologic test: the IgA tTGA.

Serologic Testing

The diagnostic approach to detecting CD has undergone important changes in recent years. Serologic tests, particularly the IgA antiendomysial antibody (EMA) and the IgA tTGA, have become a relatively sensitive and specific way to initially detect CD. The IgA tTGA is both sensitive and specific for CD and supplants the use of gliadin antibody testing as the preferred means of serologic detection. Overall, many studies demonstrate a specificity of IgA tTGA greater than 95% and a sensitivity in the range of 90% to 96%. The EMA detected by an indirect immunofluorescence assay is more time consuming and operator dependent than the tTGA. It has a slightly lower and variable sensitivity but an excellent specificity (99.6%). IgA AGA by ELISA predates the previously described serologic tests, but its diagnostic performance compared with IgA tTGA and IgA EMA is not attractive. The prevalence of IgA deficiency in CD is sufficiently low, such that the routine measurement of serum IgA levels along with IgA EMA or tTGA is not warranted as a first step toward diagnosis unless IgA deficiency is strongly suspected. In cases of selective IgA deficiency, either the IgG EMA and/or IgG tTGA have excellent sensitivity and specificity, although those IgG-based tests are markedly less sensitive and specific than the IgA-based tests in those with normal levels of IgA. Measurement of the serum IgA level is an appropriate next step in individuals with a negative IgA EMA or IgA tTGA in whom CD is still suspected. If CD is strongly suspected despite negative serologic test results, one can test for the presence of the disease-associated HLA alleles and, if present, proceed to small intestinal mucosal biopsy. Alternatively, it is reasonable to proceed directly to upper intestinal endoscopy and small bowel biopsy if the signs and symptoms that suggested CD would otherwise warrant those procedures.

Conclusion

In the primary care setting, the IgA tTGA is the most efficient single serologic test for the detection of CD. Evidence indicates that the additional inclusion of IgG AGA and IgA AGA is not warranted.

Intestinal Biopsy

Positive serologic test results are supportive of the diagnosis of CD. Distal duodenal biopsy specimens demonstrating characteristic histologic changes in the small intestinal mucosa, which includes a spectrum of change from total to partial villous atrophy, and crypt lengthening with an increase in lamina propria and intraepithelial lymphocytes, remain the gold standard for establishing the diagnosis of CD. An increase in intraepithelial lymphocytes without other

mucosal changes may represent latent CD or a part of the spectrum of gluten-sensitive enteropathy but should not be considered diagnostic of CD. It is important to take multiple (ideally 6) biopsy specimens and best to obtain these from the second part of the duodenum or beyond because mucosal changes can be patchy or Brunner's glands or peptic changes may hamper histopathologic examination if biopsy specimens are obtained from the more proximal duodenum. Gluten challenge and a repeat biopsy are no longer required to establish the diagnosis of CD in patients whose initial small intestinal biopsy specimen has the characteristic histologic appearance and in whom an objective response to a GFD is obtained. However, a gluten challenge with a subsequent biopsy does have a role in establishing the diagnosis in select clinical settings (e.g., in those with a high suspicion for CD and a negative serologic test result and who started on a GFD without biopsy confirmation of the disease). It is crucial that the dietary status of the patient at the time of biopsy be taken into account. Patients should undergo biopsy promptly after obtaining a positive serologic test result and should be instructed not to avoid gluten until after biopsy specimens are obtained. A gluten-reduced diet may reduce the severity of the lesion and impact pathologic interpretation. How long gluten must be reintroduced before biopsy specimens are taken can vary among individuals already on a GFD. A 4-week challenge with sufficient gluten to reproduce the symptoms is adequate in most. However, some patients may have very delayed responses, and it can take up to several years for relapse to occur.

Reaching a definitive diagnosis can be difficult in those with minimal histologic findings, in those with a negative serologic test result, or if the disease is patchy or an insufficient number or poorly oriented biopsy specimens were taken. There are other disease entities that can resemble CD histologically. Most of these entities are either rare in the developed world, are suggested by the clinical history, or have distinguishing histologic findings on careful review of the biopsy samples. Endoscopy provides a ready opportunity to examine the duodenal mucosa visually and to obtain a sufficient number of biopsy specimens. However, the visual examination of the small bowel mucosa is not entirely sensitive for identifying villous atrophy, although endoscopists should be aware of the visual appearance of villous atrophy. Endoscopists should not regard the absence of visual endoscopic features of CD as sufficient to rule out the diagnosis.

Use of HLA-DQ2 and -DQ8 to Exclude the Diagnosis of CD

Approximately 40% of the general population in the United States have either the HLA class II heterodimer HLADQ2 or HLA-DQ8, which reflects the presence of the DQ alleles DQA1*05 and DQB1*02 (DQ2) or DQA1*03 and DQB1*0302 (DQ8). However, almost all patients with CD have either DQ2 (~95% of patients with CD) or DQ8 (~5% of patients with CD). A very small number of patients with CD have been noted to have only DQA1*O5 or DQB1*02, the

	latter usually being associated with HLA-DR7 heterozygosity or homozygosity. Because virtually all patients with CD have the CD-associated alleles mentioned previously at the DQA1 and DQB1 loci, the absence of these alleles provides a negative predictive value for the disease of close to 100% (i.e., if individuals lack the relevant disease-associated alleles, CD is virtually excluded). HLA testing for the relevant DQ alleles can be a useful adjunct in an exclusionary sense when the diagnosis based on other tests is not clear. When using HLA testing in the context of disease susceptibility in families, one must have the resources available to provide genetic counseling.

NICE (2009)	**Dietary Considerations Before Testing for CD**
	
	• Do not use serological testing for CD in infants before gluten has been introduced to the diet.
	• Inform people (and their parents or carers, as appropriate) that any testing for CD is accurate only if the person continues to follow a gluten-containing diet during the diagnostic process (serological tests and biopsy if required).
	• Inform people that they should not start a GFD until diagnosis is confirmed by intestinal biopsy, even if a self-test or other serological test is positive.
	• Inform people that when they are following a normal diet (containing gluten) they should eat some gluten (for example, bread, chapattis, pasta, biscuits, or cakes) in more than one meal every day for a minimum of 6 weeks before testing; however, it is not possible to say exactly how much gluten they should eat.
	• If a person is reluctant or unable to reintroduce gluten into their diet before testing:
	  • Refer them to a gastrointestinal specialist
	  • Inform them that it may be difficult to confirm a diagnosis of CD on intestinal biopsy, and that this may have implications for the prescribing of gluten-free foods.
	
	Other Information Before Serological Testing
	
	• Inform people who are considering, or have undertaken, self-testing for CD (and their parents or carers) that any result from self-testing needs to be discussed with a healthcare professional and confirmed by laboratory-based tests.
	• Before seeking consent to take blood for serological tests, explain:
	  • What CD is
	  • That serological tests do not diagnose CD, but indicate whether further testing is needed
	  • The implications of a positive test (including referral for intestinal biopsy and implications for other family members)

	• The implications of a negative test (that CD is unlikely but it could be present or could arise in the future) • Inform people and their parents or carers that a delayed diagnosis of CD, or undiagnosed CD, can result in: • Continuing ill health • Long-term complications, including osteoporosis and increased fracture risk, unfavourable pregnancy outcomes and a modest increased risk of intestinal malignancy • Growth failure, delayed puberty and dental problems (in children) **Serological Tests** • All tests should be undertaken in laboratories with clinical pathology accreditation (CPA). • Do not use IgG or IgA AGA tests in the diagnosis of CD. • Do not use of self-tests and/or point-of-care tests for CD as a substitute for laboratory-based testing. • When clinicians request serology, laboratories should: • Use IgA tTGA as the first choice test • Use IgA EMA testing if the result of the tTGA test is equivocal • Check for IgA deficiency if the serology is negative* • Use IgG tTGA and/or IgG EMA serological tests for people with confirmed IgA deficiency • Communicate the results clearly in terms of values, interpretation and recommended action. *Investigation for IgA deficiency should be done if the laboratory detects a low or very low optical density on IgA tTGA test or low background on IgA EMA test. • Do not use HLA DQ2/DQ8 testing in the initial diagnosis of CD. (However, its high negative predictive value may be of use to gastrointestinal specialists in specific clinical situations.) **After Serological Testing** • Offer referral to a gastrointestinal specialist for intestinal biopsy to confirm or exclude CD to people with positive serological results from any tTGA or EMA test. • If serology tests are negative but CD is still clinically suspected, offer referral to a gastrointestinal specialist for further assessment.
WGO-OMGE (2007)	**Diagnostic Tests** Only endoscopy with biopsy of the small intestine plus a positive CD serology provide a definitive diagnosis. This is the gold standard. (See the algorithm in the original guideline document on diagnosis of

CD.)

Role of Endoscopy for Suspicion of CD

Although endoscopy may provide an indication for intestinal biopsy, it may not be sufficiently sensitive to detect all manifestations of CD in a population.

The characteristic findings of an endoscopy include:

- Scalloped folds, fissures and mosaic pattern
- Flattened folds
- Smaller size and or disappearing of folds with maximum insufflation

Intestinal Biopsy

Intestinal biopsies together with a positive serology represent the gold standard for diagnosing CD.

Multiple biopsies are taken from the second or third part of the duodenum. Endoscopy has become the most convenient method of obtaining biopsies of the small-intestinal mucosa. Suction biopsy (Crosby capsule) provides the best samples.

Histological Characteristics of Celiac Enteropathy

CD affects the mucosa of the proximal small intestine, with damage gradually decreasing in severity towards the distal small intestine, although in severe cases the lesions can extend to the ileum. The degree of proximal damage varies greatly depending on the severity of the disease. The proximal damage may be very mild in "silent" cases, with little or no abnormality detectable histologically in the mid-jejunum. Abnormalities in the gastric and rectal mucosa may be observed in some cases.

Occasionally, the lesion in the duodenum/upper jejunum can be patchy, which may justify a second biopsy immediately in selected patients with positive endomysial antibody (EMA). However, this is only warranted if all three samples of the first biopsy show a normal histology.

Use of Serum Antibodies to Diagnose CD

- IgA EMA; highest diagnostic accuracy
- IgA tTG
- IgA AGA
- IgG AGA

Serologic studies for CD can be divided into two groups, based on

the target antigens:

- Anti-tTG antibody tests
- AGA tests

IgA EMA. IgA endomysial antibodies bind to endomysium, the connective tissue around smooth muscle, producing a characteristic staining pattern that is visualized by indirect immunofluorescence.

The test result is reported simply as positive or negative, since even low titers of serum IgA endomysial antibodies are specific for CD. The target antigen has been identified as tissue transglutaminase (tTG or transglutaminase 2).

IgA endomysial antibody testing is moderately sensitive and highly specific for untreated (active) CD.

Anti-tissue transglutaminase antibodies (IgA tTG). The antigen against which antiendomysial antibodies are directed is tTG. Anti-tTG antibodies are highly sensitive and specific for the diagnosis of CD.

ELISA tests for IgA anti-tTG antibodies are now widely available and are easier to perform, less observer-dependent and less costly than the immunofluorescence assay used to detect IgA endomysial antibodies. The diagnostic accuracy of IgA anti-tTG immunoassays has been improved further by the use of human tTG in place of the nonhuman tTG preparations used in earlier immunoassay kits.

AGA assays (IgA AGA and IgG AGA). Gliadins are the major proteins of the wheat storage proteins collectively termed gluten.

Purified gliadin is readily available and is used as the antigen for ELISA tests to detect serum antigliadin antibodies.

Serum AGA levels are frequently elevated in untreated CD, and antigliadin assays have been used for some years as a diagnostic aid.

Although these tests demonstrate moderate sensitivity and specificity, with the IgA tests being superior, their positive predictive value in the general population is relatively poor.

AGA tests are no longer routinely recommended, because of their lower sensitivity and specificity.

The Global Aspect

The diagnosis of CD can be made with different diagnostic technologies in different parts of the world, depending on the available resources, but the specificity and validity of the results may

	vary when tools poorer than those of the "gold standard" are used. Depending on available resources, diagnostic options can be cascaded from a highly resourced setting in which the above gold standard can be used — endoscopy followed by small-bowel biopsy and specific serology for confirmation or case finding — to a situation in which very few resources are available and only the minimum can be done. If biopsy is not available, "serology only" remains a feasible method for diagnosing CD, also because serological tests are cheaper than endoscopy and biopsy and their statistical value is very similar. In the absence of a biopsy, the criteria are: • The presence of auto-antibodies • Gluten dependency of the auto-antibody titer • Clinical symptoms, when present • Improvements in symptoms and reduction in the anti-tTG antibody titer on a GFD • In children, catch-up growth, when applicable The easiest and cheapest serological test would be the dot ELISA. Once a bedside IgA anti tTG test becomes available and sufficiently sensitive and specific, it would be ideal for low-income regions. If a geographic area has very limited resources, clinical aspects become the most important diagnostic tool. A rice-based or corn-based GFD is the final and vital step in confirming a diagnosis of CD. Although endoscopy is a very useful tool for detecting CD, it cannot be relied on as a single diagnostic procedure. The presence of markers of mucosal atrophy may be highly suggestive of CD be in places where the disease is common, but in other areas of the world there may be several differential diagnoses — for example, tropical sprue, malnutrition, heavy-chain disease, etc. Nevertheless, the procedure is very helpful when markers are elevated in the course of endoscopies ordered for other reasons. Then the endoscopist must be alert and proceed to intestinal biopsy.
MANAGEMENT **Abbreviations** **Back to TOC**	
ADA (2009)	**MNT** MNT provided by a RD is strongly recommended for individuals with CD. Consultation with a RD as part of a team-based approach results

in improved self-management.

Consensus, Imperative

Assessment of Food/Nutrition-Related History

The RD should assess the food and nutrition-related history of individuals with CD, including (but not limited to) the following:

- Food and nutrient intake (e.g., diet history, diet experience and macronutrient or micronutrient intake, specifically calcium, iron, vitamin B complex and vitamin D)
- Medication and herbal supplement use
- Knowledge, beliefs or attitudes (e.g., readiness to change nutrition-related behaviors)
- Behavior (e.g., social network)
- Factors affecting access to food and food and nutrition-related supplies (e.g., safe food and meal availability)

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition intervention. Intake of gluten results may result in gastrointestinal symptoms, malabsorption and villous atrophy.

Strong, Imperative

Assess Factors Affecting Quality of Life

The RD should assess the factors affecting the quality of life of individuals with CD when completing a comprehensive client history, which includes a medical history (e.g., gastrointestinal, immune, neurological and psychological) and social history (e.g., socioeconomic factors, religion, social and medical support and daily stress level). Individuals with CD may not attain the same level of quality of life as the general population, due to social inconveniences of following a gluten-free dietary pattern.

Strong, Imperative

Bone Density Screening

The RD should recommend bone density screening for adults with CD within the first year. Clinical trials and cross-sectional studies have reported reduced bone mineral content and BMD in untreated adults with CD.

Strong, Conditional

Assess Biochemical Data and Results of Medical Procedures

The RD should assess the biochemical data and review the results of medical procedures in individuals with CD, regardless of presentation and clinical symptoms, including (but not limited to) the following:

- Gastrointestinal profile (e.g., intestinal biopsy [or skin biopsy in the case of dermatitis herpetiformis] and celiac antibodies)
- Nutritional anemia profile (e.g., folate, ferritin and vitamin B12)
- Vitamin profile (e.g., thiamin, vitamin B6 and 25-hydroxy vitamin D)
- Mineral profile (e.g., copper and zinc)
- Lipid profile
- Electrolyte and renal profile

Untreated CD results in villous atrophy and malabsorption. The use of effective techniques to assess nutritional status is essential to prevention and treatment of malnutrition and the presence of iron deficiency anemia.

Strong, Imperative

Assess Gastrointestinal Symptoms

The RD should assess gastrointestinal symptoms (such as type, frequency and volume of bowel function; abdominal pain and bloating; nausea or vomiting; reduced gut motility and delayed gastric emptying) in individuals with CD. Several studies have reported that people with CD (treated and untreated) are more likely to experience gastrointestinal symptoms than are healthy control subjects.

Strong, Imperative

Assessment of Other Disease States

The RD should assess for the presence of other disease states, such as thyroid conditions, other autoimmune and endocrinologic disorders and diabetes, when implementing MNT. Identification of all nutritional issues is optimal to integrate MNT for individuals with CD into overall disease management.

Consensus, Imperative

Inclusion of Gluten-Free Oats as Tolerated

The RD should advise individuals with CD who enjoy and can tolerate gluten-free oats to gradually include them in their gluten-free dietary pattern. Research on individuals with CD reports that incorporating oats uncontaminated with wheat, barley or rye at intake levels of

approximately 50g dry oats per day is generally safe and improves compliance with the gluten-free dietary pattern.

Fair, Conditional

Consumption of Whole/Enriched Gluten-Free Grains and Products

The RD should advise individuals with CD to consume whole or enriched gluten-free grains and products such as brown rice, wild rice, buckwheat, quinoa, amaranth, millet, sorghum, teff, etc. Research reports that adherence to the gluten-free dietary pattern may result in a diet that is low in carbohydrates, iron, folate, niacin, zinc and fiber.

Strong, Imperative

Addition of Multivitamin and Mineral Supplement

If usual food intake shows nutritional inadequacies that cannot be alleviated through improved eating habits, the RD should advise individuals with CD to consume a daily gluten-free age- and sex-specific multivitamin and mineral supplement. Research reports that adherence to the gluten-free dietary pattern may result in a diet that is low in iron, folate, niacin, vitamin B12, calcium, phosphorus and zinc.

Strong, Conditional

Calcium/Vitamin D for Reduced Bone Density

For adults with reduced bone density or reduced serum levels of 25-hydroxyvitamin D, the RD should advise the consumption of additional calcium and vitamin D through food or gluten-free supplements. Studies in adults with untreated CD have shown that a gluten-free dietary pattern improves, but may not normalize BMD.

Strong, Conditional

Iron Supplementation for Iron Deficiency Anemia

For individuals with iron deficiency anemia and CD, the RD should advise the consumption of a daily gluten-free multivitamin with iron or additional individualized therapeutic doses of iron. Studies report that iron supplementation may be necessary to achieve normal values of hematological parameters.

Strong, Conditional

	<u>Gluten-Free Dietary Pattern</u> The RD should advise and educate individuals with CD to be compliant with a gluten-free dietary pattern. Research on individuals with CD reports that long-term compliance with a gluten-free dietary pattern improves outcomes related to bone density, iron deficiency anemia, villous atrophy, gastrointestinal and neurological symptoms, pregnancy outcomes and quality of life. **Strong**, Imperative **<u>Provide Resources and Education on Label Reading</u>** The RD should provide resources and educate individuals with CD about reviewing the ingredients on labels of food and supplements, using current publications, including those from the United States Food and Drug Administration, for identification and avoidance of sources of gluten, namely wheat, rye, barley, malt and oats (unless oats are gluten-free). Education about the disease is optimal to integrate MNT for individuals with CD into overall disease management. **Consensus**, Imperative **<u>Education on Food Cross-Contamination</u>** The RD should educate individuals with CD regarding cross-contamination in gluten-free food preparation within manufacturing plants, restaurants and home kitchens. Education about the disease is optimal to integrate MNT for individuals with CD into overall disease management. **Consensus**, Imperative **<u>Coordination of Care</u>** The RD should implement MNT and coordinate nutrition care with a team of clinical professionals. Depending on the coexisting conditions of the individual with CD, consultation with gastroenterologists, endocrinologists, allergists, dermatologists, hepatologists, pharmacists, social workers, etc., may be warranted. An interdisciplinary team approach is optimal to integrate MNT for individuals with CD into overall disease management. **Consensus**, Imperative
AGA (2006)	Treatment of CD requires a strict, lifelong adherence to a GFD. This is also the case for patients with dermatitis herpetiformis. Clinicians need to ensure that patients have adequate education, motivation, and support to achieve this diet. Consultation with an experienced

	dietician, referral to a support group, and clinical follow-ups for compliance are recommended. Treatment of nutritional deficiency states (e.g., iron, folate, vitamin B12) is essential, and a determination of BMD to assess for osteoporosis is recommended. **Promoting Adherence to a GFD** Changes in dietary habits are difficult to maintain, and there are many barriers to continued compliance with a GFD. Improved knowledge of CD, the GFD, gluten-containing food products, and outcomes of untreated CD would likely improve compliance. Membership in a local celiac society provides patients with CD with improved knowledge regarding their disease, the intricacies of the GFD, and also emotional and social support opportunities. **Expected Benefits of a GFD** Compliance with a GFD is likely protective against the development of non-Hodgkin's lymphoma in CD and dermatitis herpetiformis. There is compelling evidence that treatment of symptomatic CD results in substantial improvement in nutritional parameters. The treatment of CD with a GFD can result in improvements in BMD, with the greatest improvements appearing in the first years of the GFD. Treatment with a GFD for at least 12 months can result in increased body weight, body mass index, fat mass, bone mass, triceps skin fold thickness, and nutritional and biochemical status including iron absorption. Patients adhering to a strict GFD usually consume fewer calories than noncompliers but show a trend toward greater improvements in measurements of body composition. The benefits of a GFD on short-term outcomes in diabetic patients with CD are inconclusive. They suggest that nutritional parameters can improve but no convincing change in diabetic control has been demonstrated, although insulin requirements often increase.
NICE (2009)	No recommendations offered.
WGO-OMGE (2007)	**Management** The current treatment for CD is a strictly GFD for life. In the GFD, wheat, barley, and rye are avoided. Oats are not toxic in > 95% of patients with CD or dermatitis herpetiformis, but there is a small subgroup (< 5%) for whom oats are not safe. Additionally, there is a reluctance in some countries to advise liberal use of oats because of the difficulty in guaranteeing that commercially available oats will be free of contamination with other grains. Rice and corn can be part of a GFD.

Initial approach:

- Prescribe a "natural" GFD
- Refer to a dietician and/or support group (see web sites listed below)
- Screen for iron and folate deficiency
- Advise bone-density tests (in some cases)
- Advise vitamin D and calcium supplementation if the patient is osteoporotic
- Advise serological screening for first-degree and second-degree relatives

Most patients have a rapid clinical response to a GFD (within 2 weeks), although the rate of response varies. Patients who are extremely ill may require hospital admission, repletion of fluids and electrolytes, intravenous alimentation, and, occasionally, steroids. Patients should be encouraged to eat natural high-iron and high-folate foods, especially if a deficiency in these minerals is documented.

Patients should also have a consultation with a dietician who is knowledgeable about GFDs. However, not all dieticians are familiar with the intricacies of a GFD, and for this reason local or national support groups provide most of the required information.

For adults, quality of life is improved on a GFD, even in those whose disease was detected by screening. Children on a GFD reported a quality of life comparable to that of a reference population. Adolescents have difficulty with dietary compliance.

(Refer to Table 5 in the original guideline document for foods allowed in a GFD)

The GFD

The most effective treatment is a rigorous GFD for life. This means no wheat, rye, or barley. Oats — provided they are pure and not contaminated with other grains (even minimal amounts of wheat, rye or barley) — are safe to eat in > 95% of cases.

Plain meat, fish, rice, corn, fruits, and vegetables do not contain gluten. Examples of foods that are safe to eat and those that are not can be found online. Useful online CD information sites are listed in sections 8 and 9 of the original guideline document.

A GFD is low in fiber. Patients should be advised to eat a high-fiber diet supplemented with whole-grain rice, maize, potatoes and ample vegetables.

Correct any dietary deficiencies such as iron, folic acid, calcium and

	(very rarely) B_{12} deficiency.

FOLLOW-UP/PERSISTENCE OF SYMPTOMS **Abbreviations** **Back to TOC**	
ADA (2009)	**Monitoring and Evaluation of Dietary Compliance** The RD should monitor the following to evaluate dietary compliance: • Gluten-free dietary pattern • Antibody levels • Potential exposure to cross-contamination • Hidden sources of gluten in foods, medications and supplements Intake of gluten may result in gastrointestinal symptoms, malabsorption and villous atrophy. **Strong**, Imperative **Monitoring and Evaluation of Factors Affecting Quality of Life** The RD, at every encounter, should monitor and evaluate the factors affecting the quality of life of individuals with CD, reviewing changes in client status, which includes medical status (e.g., gastrointestinal, immune, neurological and psychological) and social status (e.g., socioeconomic factors, religion, social and medical support and daily stress level). Individuals with CD may not attain the same level of quality of life as the general population, due to social inconveniences of following a gluten-free dietary pattern. **Strong**, Imperative **Monitoring and Evaluation of Gastrointestinal Symptoms** The RD, after ruling out gluten exposure, should monitor and evaluate persistent gastrointestinal symptoms in individuals with CD, such as bloating, gas, constipation and diarrhea, as there may be other potential causes, such as leaky gut, lactose, fructose and carbohydrate intolerances, bacterial overgrowth, refractory sprue, related cancers, and other gastrointestinal diseases and conditions. Several studies have reported that people with CD (treated and untreated) are more likely to experience gastrointestinal symptoms than healthy controls; compliance with a GFD reduces but may not eliminate these symptoms. **Fair**, Imperative

AGA (2006)	**Promoting Adherence to a GFD** Follow-up is necessary to confirm the diagnosis by an objective response to a GFD and to detect and manage noncompliance. Patients with CD should be evaluated at regular intervals by a health care team including a physician and a dietician. These visits can be used to assess, by history, a patient's compliance with a GFD and to reinforce the importance of such compliance. Beyond this, there are no clear guidelines as to the optimal means to monitor adherence to a GFD. In general, monitoring adherence to a GFD with serologies (i.e., tTGA or EMA) is sensitive for major but not for minor transient dietary indiscretions. In children, histologic improvement on a GFD appears to occur quickly, while in adults the small intestinal mucosa heals more slowly and less completely. Monitoring adherence by clinic visits and serologic testing appears to be a reasonable approach in children. In adults, this approach is also reasonable with the understanding that a negative serologic test result does not necessarily mean improvement beyond severe subtotal or total villous atrophy. **Nonresponsive CD** Patients with known CD can continue to have or can redevelop symptoms despite being on a GFD. These symptoms may be due to incompletely healed CD, an associated condition, a complication, or a second unrelated diagnosis. Persistent or intermittent symptoms due to known or inadvertent ingestion of gluten are commonly reported. If gluten ingestion is not suggested by direct review of the dietary history or positive serologic test result, then a careful search should be undertaken for other entities such as microscopic colitis, pancreatic exocrine insufficiency, bacterial overgrowth, and disaccharidase deficiency. Intestinal lymphoma, small bowel strictures, or true refractory sprue should be considered in the absence of these and in persistently febrile or very ill patients. Refractory sprue is a rare entity with a high morbidity and mortality and is defined as continued or recurrent malabsorption and diarrhea associated with persisting moderate or severe villous atrophy despite adherence to a strict GFD. The evaluation of these patients should include a careful evaluation for coexistent T-cell lymphomas. The optimal therapy for celiac sprue is not known but frequently includes immunosuppression.
NICE (2009)	No recommendations offered.
WGO-OMGE (2007)	**Persistence of Symptoms** A common difficulty with the GFD is the presence of occult gluten in processed foods and/or medicines (although this is rare). The

	persistence of symptoms is almost always caused by continued ingestion of gluten. Reasons for persistence of symptoms: • (Inadvertent) gluten ingestion (this is the most common reason) • Wrong diagnosis • Lactose or fructose intolerance • Other food intolerances • Pancreatic insufficiency • Microscopic colitis • Bacterial overgrowth • Collagenous colitis or collagenous sprue • Irritable bowel syndrome • Ulcerative jejunitis • Enteropathy-associated T-cell lymphoma • Refractory CD The last three can be regarded as complications of long-lasting CD. **Refractory CD** The diagnosis of refractory CD is considered in patients with features of CD who have persistent symptoms, villous atrophy, and failure to respond to a GFD. This may occur at presentation, or after an initial response to a GFD. Refractory CD is considered to be a form of low-grade intraepithelial lymphoma, revealed by severe malabsorption that is not responsive to a GFD. This diagnosis must be considered particularly in CD patients who are diagnosed over the age of 50.

STRENGTH OF EVIDENCE AND RECOMMENDATION GRADING SCHEMES

Abbreviations
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ADA (2009)

Levels of Evidence

Strength of Evidence Elements	Grade I Good/Strong	Grade II Fair	Grade III Limited/Weak	Grade IV Expert Opinion Only

Quality • Scientific rigor/validity • Considers design and execution	Studies of strong design for question Free from design flaws, bias and execution problems	Studies of strong design for question with minor methodological concerns OR Only studies of weaker study design for question	Studies of weak design for answering the question OR Inconclusive findings due to design flaws, bias or execution problems	No studies available Conclusion based on usua practice, exper consensus, clinical experience, opinion, or extrapolation from basic research
Consistency Of findings across studies	Findings generally consistent in direction and size of effect or degree of association, and statistical significance with minor exceptions at most	Inconsistency among results of studies with strong design OR Consistency with minor exceptions across studies of weaker designs	Unexplained inconsistency among results from different studies OR Single study unconfirmed by other studies	Conclusion supported solely by statements of informed nutrition or medical commentators
Quantity • Number of studies • Number of subjects in studies	One to several good quality studies Large number of subjects studies Studies with negative results having sufficiently large sample size for adequate statistical power	Several studies by independent investigators Doubts about adequacy of sample size to avoid Type I and Type II error	Limited number of studies Low number of subjects studies and/or inadequate sample size within studies	Unsubstantiate by published studies
Clinical Impact • Importance of studied outcomes	Studied outcome relates directly to the question	Some doubt about the statistical or clinical significance of	Studies outcome is an intermediate outcome or surrogate for	Objective data unavailable

• Magnitude of effect	Size of effect is clinically meaningful Significant (statistical) difference is large	effect	the true outcome of interest OR Size of effect is small or lacks statistical and/or clinical significance	
Generalizability To population of interest	Studied population, intervention and outcomes are free from serious doubts about generalizability	Minor doubts about generalizability	Serious doubts about generalizability due to narrow or different study population, intervention or outcomes studied	Generalizabilit limited to scop of experience

This grading system was based on the grading system from: *Greer N, Mosser G, Logan G, Wagstrom Halaas G. A to evidence grading. Jt Comm. J Qual Improv. 2000; 26:700-712*. In September 2004, The ADA Research Comm grading system to this current version.

Criteria for Recommendation Rating

Statement Rating	Definition	Implication for Pr
Strong	A **Strong** recommendation means that the workgroup believes that the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation), and that the quality of the supporting evidence is excellent/good (grade I or II)*. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Practitioners should follow a recommendation unless a cle compelling rationale for an a approach is present.
Fair	A **Fair** recommendation means that the workgroup believes that the benefits exceed the harms (or that the harms clearly exceed the benefits in the case of a negative recommendation), but the quality of evidence	Practitioners should generally recommendation but remain information and be sensitive preferences.

		is not as strong (grade II or III)*. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	
	Weak	A **Weak** recommendation means that the quality of evidence that exists is suspect or that well-done studies (grade I, II, or III)* show little clear advantage to one approach versus another.	Practitioners should be cauti whether to follow a recomme classified as **Weak**, and shou judgment and be alert to em publications that report evide preference should have a sub influencing role.
	Consensus	A **Consensus** recommendation means that Expert opinion (grade IV)* supports the guideline recommendation even though the available scientific evidence did not present consistent results, or controlled trials were lacking.	Practitioners should be flexib whether to follow a recomme classified **Consensus**, althou set boundaries on alternative preference should have a sub influencing role.
	Insufficient Evidence	An **Insufficient Evidence** recommendation means that there is both a lack of pertinent evidence (grade V)* and/or an unclear balance between benefits and harms.	Practitioners should feel little deciding whether to follow a recommendation labeled as I **Evidence** and should exercis be alert to emerging publicat evidence that clarifies the ba versus harm. Patient prefere a substantial influencing role
	*Conclusion statements are assigned a grade based on the strength of the evidence. Grade I is good; grade II, f limited; grade IV signifies expert opinion only and grade V indicates that a grade is not assignable because there support or refute the conclusion. The evidence and these grades are considered when assigning a rating (Strong Consensus, Insufficient Evidence - see chart above) to a recommendation. Adapted by the American Dietetic Association from the American Academy of Pediatrics, Classifying Recommend Practice Guideline, Pediatrics. 2004;114;874-877.		
AGA (2006)	Not applicable		
NICE (2009)	Not applicable		
WGO-OMGE (2007)	Not applicable		

COMPARISON OF METHODOLOGY *Click on the links below for details of guideline development methodology*			
ADA (2009)	**AGA (2006)**	**NICE (2009)**	**WGO-OMGE (2007)**
To collect and select the evidence, all four groups performed searches of electronic databases; ADA, NICE and WGO-OMGE also performed hand-searches of published literature (primary sources). In addition, NICE performed hand-searches of published literature (secondary sources) and searches of unpublished data. All of the groups provide a description of the literature collection/selection process. Expert consensus was employed by all four groups as a method of assessing the quality and strength of the evidence. In addition, ADA also weighted the evidence according to a rating scheme and provide the scheme. To analyze the evidence, AGA performed a review; ADA and NICE performed a systematic review with evidence tables and all describe the process. WGO-OMGE performed a review (including meta-analyses), but does not describe the process(es) used. The three groups to provide information regarding the recommendation formulation process, AGA, ADA and NICE, utilized expert consensus. Informal consensus was also used by NICE. These three groups provide a description of the recommendation formulation process. ADA is the only group to rate the strength of its recommendations according to a rating scheme. With regard to issues of cost-effectiveness, ADA performed an analysis of potential costs associated with the application of its recommendations. NICE conducted a literature review to identify evidence on the cost-effectiveness of serological tests for celiac disease. Because of the lack of published economic evidence that fully addresses the cost effectiveness of serological testing in the decision-making context of this guideline, the NICE Guideline Development Group (GDG) requested the development of a de novo model to estimate the cost effectiveness of serological test strategies for detecting celiac disease in patients presenting with signs and symptoms. AGA and WGO-OMGE neither performed a formal cost analysis nor reviewed published cost analyses. The three groups to provide information regarding guideline validation, ADA, AGA and NICE, all sought internal peer review. ADA and NICE also sought external peer review. All three groups provide details of the process.			

SOURCE(S) OF FUNDING Abbreviations Back to TOC	
ADA (2009)	American Dietetic Association
AGA (2006)	American Gastroenterological Association Institute

NICE (2009)	National Institute for Health and Clinical Excellence
WGO-OMGE (2007)	World Gastroenterology Organisation

BENEFITS AND HARMS **Abbreviations** **Back to TOC**	
Benefits	
ADA (2009)	• A primary goal of implementing these recommendations is to provide MNT guidelines for Celiac Disease to promote optimal health, prevent and treat malabsorption/malnutrition and other comorbidities and improve quality of life. Potential benefits include a person's ability to achieve optimal nutrition. • Although costs of MNT sessions and reimbursement vary, MNT is essential for improved outcomes. MNT education can be considered cost effective when considering the benefits of nutrition interventions on the onset and progression of comorbidities versus the cost of the intervention. • Dietetic practitioners, patients, and consumers may make shared decisions about health care choices; if properly communicated and implemented, this guideline can improve care.
AGA (2006)	**Overall Benefits** Appropriate diagnosis and management of CD **Specific Benefits** • Compliance with a GFD is likely protective against the development of non-Hodgkin's lymphoma in CD and dermatitis herpetiformis. • There is compelling evidence that treatment of symptomatic CD results in substantial improvement in nutritional parameters. The treatment of CD with a GFD can result in improvements in BMD, with the greatest improvements appearing in the first years of the GFD. Treatment with a GFD for at least 12 months can result in increased body weight, body mass index, fat mass, bone mass, triceps skin fold thickness, and nutritional and biochemical status including iron absorption. Patients adhering to a strict GFD usually consume fewer calories than noncompliers but show a trend toward greater improvements in measurements of body composition. • Making the diagnosis at a young age, educating patients and

	parents, and utilizing a multidisciplinary approach to patient management and follow-up would be expected to improve compliance and patient outcomes.
NICE (2009)	Effective recognition and assessment of celiac disease in order to provide satisfactory individual treatment and to improve the overall health of the community
WGO-OMGE (2007)	Improved diagnosis and management of CD to reduce disease-associated morbidity and improve quality of life
Harms	
ADA (2009)	**Overall Risk/Harm Considerations** When using these recommendations: • Review the patient's age, socioeconomic status, cultural issues, health history, and other health conditions. • Consider referral to other specialties: Allergy and Immunology, Endocrinology, Gastroenterology, Hematology, Neurology, Obstetrics and Gynecology, Pediatrics, Family Practice, Rheumatology. • Consider referral to a behavioral specialist if psychosocial issues are a concern. • Consider a referral to social services to assist patients with financial arrangements if economic issues are a concern. • Use clinical judgment in applying the guidelines when evaluating patients with celiac disease. • Give careful consideration to the application of these guidelines for patients with significant comorbidities. In addition to the above, a variety of barriers may hinder the application of these recommendations. **Recommendation-Specific Risks/Harms** *Inclusion of Gluten-Free Oats* • In a small number of persons with celiac disease, research reports that oats may cause villous atrophy, an increase in intraepithelial lymphocytes or exacerbate dermatitis herpetiformis. • The introduction of oats may result in gastrointestinal symptoms such as diarrhea and abdominal discomfort. These symptoms may be due to an increase in fiber intake and not be a sign of intolerance to oats.

	Meeting Nutritional Needs • Consumption of Whole/Enriched Gluten-Free Grains and Products: Individuals who are newly diagnosed or unaccustomed to a higher fiber diet may need to introduce gluten-free whole grains and products gradually into their gluten-free dietary pattern. • Addition of Multivitamin and Mineral Supplement: Consumption of nutrients exceeding the upper limit of the Dietary Reference Intakes (DRIs) may lead to adverse condition. *Iron Supplementation* • Consumption of iron beyond the tolerable upper intake level (UL) may result in hemochromatosis. *Gluten-Free Dietary Pattern* • Compliance with a gluten-free dietary pattern before confirmed diagnosis of celiac disease may result in inaccurate diagnostic results. *Providing Resources and Education on Label Reading* • Careful attention must be given to label-reading education. Incomplete or absence of detailed label reading education could result in consumption of products that may contain gluten-containing ingredients. • Individual need to be instructed on continued monitoring of product labels and ingredients, as manufacturers may periodically change ingredients. • Incomplete implementation of label-reading education recommendation may result in liability issues. *Education on Cross-Contamination* • Careful attention must be given to education on cross-contamination to help prevent individuals with celiac disease from unintentionally consuming gluten.
AGA (2006)	Not stated
NICE (2009)	Not stated
WGO-OMGE (2007)	False positive and false negative diagnostic tests

CONTRAINDICATIONS Abbreviations Back to TOC	
ADA (2009)	• Clinical judgment is crucial in the application of these guidelines. Careful consideration should be given to the application of these guidelines for patients with significant medical co-morbidities. • Bone density screening may be contraindicated in pregnancy. • The Consumption of Whole/Enriched Gluten-Free Grains and Products recommendation may be contraindicated in individuals who are on a fiber-restricted diet
AGA (2006)	Not stated
NICE (2009)	Not stated
WGO-OMGE (2007)	Not stated

Abbreviations
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ADA, American Dietetic Association

AGA, antigliadin antibody

AGA Institute, American Gastroenterological Association Institute

BMD, bone mineral density

CD, celiac disease

ELISA, enzyme-linked immunosorbent assay

EMA, antiendomysial antibody

GFD, gluten-free diet

HLA, human leukocyte antigen

IgA, immunoglobulin A

igG, immunoglobulin G

MNT, medical nutrition therapy

NICE, National Institute for Health and Clinical Excellence

RD, registered dietitian

tTGA, tissue transglutaminase antibody

WGO-OMGE, World Gastroenterology Organisation

This synthesis was prepared by ECRI on September 7, 2007. The information was reviewed by AGA on September 14, 2007, and by WGO-OMGE on October 2, 2007. This synthesis was updated in February 2010 to remove NIH recommendations and to add ADA and NICE recommendations. The information was verified by ADA on April 5, 2010.

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